engrafted slowly, after Day 42, perhaps related to some underlying marrow dysfunction caused by MDS. Four patients developed acute GvHD grades II-IV with a cumulative incidence at 100 Days of 16.7% (95% CI 1.4%-32.0%). Four patients relapsed with a CI of relapse at 3 years of 15.0% (95% CI 0.0%-31.5%). Cumulative incidence of non-relapse mortality at 1 year was 26.1% (95% CI 7.7%-44.5%). Nine pts died: 4 of infections (2 EBV, 1 adenovirus, 1 toxoplasmosis), 2 of graft failure, 2 of relapse, and 1 of MSOF. Overall survival probability at 1 and 3 years were 70.4% (95% CI 51.9%-88.8%) and 59.5% (95% CI 38.7%-80.4%) respectively. Event-free survival (EFS) probabilities at 1 and 3 years were 70.8% (95% CI 52.6%-89.0%) and 59.9% (39.2%-80.7%), respectively. Factors associated with better EFS were age $\leq$ 10 years ($p = 0.03$) and weight $\leq$ 38 kg ($p = 0.02$). These results, especially in younger patients with Monosomy 7 and MDS, are equivalent to matched allogeneic bone marrow transplant data. UCB should be actively considered for pediatric MDS patients lacking matched related or unrelated adult donors.

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THE ADDITION OF ETOPOSIDE TO Bu_{16}/Cy_{200} IN THE CONDITIONING OF CHILDREN WITH ACUTE MYELOID LEUKEMIA (AML) UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION (SCT) IS ASSOCIATED WITH IMPROVED SURVIVAL

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Relapse remains the major concern for children with AML undergoing SCT, and we have previously shown that intensifying the conditioning by adding etoposide at 60 mg/kg and consequently reducing the busulfan (Bu) dose to 12 mg/kg and the cytoxan (Cy) to 90 mg/kg did not result in any significant improvement of the survival; we suggested then that the reduction of Bu/Cy doses necessitated by addition of the high dose of etoposide could have affected the outcome and we hypothesized that adding a lower dose of etoposide and keeping the Bu/Cy at the conventional doses may offer better survival to AML patients undergoing allogeneic SCT. We present here our results using such a protocol.

Patients and Methods: From March 2003 until December 2006, 33 patients with AML (24 in CR1, 8 in CR 2) underwent allogeneic SCT and were conditioned with Bu 16 mg/kg po, Cy 200 mg/kg iv plus etoposide 900 mg/m^2 iv, median age was 9.6 years. This cohort of patients (group B) was compared with 18 AML patients (17 in CR 1, 1 in CR 2) who underwent SCT from July 93 thru February 96, median age at SCT was 7.25 years, patients were conditioned with only Bu 16 mg/kg po and Cy 200 mg/kg iv (group A). **Results:** Median days to ANC $\geq 500 \times 10^6$/l was 21 days and 15 days in groups A and B respectively, median days to platelet count $\geq 20 \times 10^9$/l was 22 days and 26 days in groups A and B respectively (P= NS). The incidence of complications was similar, acute GVHD grade 2 or higher developed in 5% and 9% in groups A and B respectively (P= NS), hemorrhagic cystitis developed in 11% and 15% in groups A and B respectively, no VOD developed in either group. The 4 year overall survival for groups A and B respectively was 50% and 68.2% ($P = 0.3$) and the 4 year event-free survival for groups A and B respectively was 33% and 68.2% ($P = 0.1$). **Conclusions:** The addition of etoposide to Bu_{16}/Cy_{200} was not associated with increased toxicity, and although it did not reach statistical significance, it does appear to be associated with a better overall and event-free survival. Larger scale studies are advised to further corroborate our findings.

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SINGLE DAILY DOSE (SDD) BUSULFAN (BU) IN CHILDREN: COMPARISON OF PHARMACOKINETICS (PK) AND ENGRAFTMENT BETWEEN ACUTE LEUKAEMIA (AL) AND NON MALIGNANT DISEASE (NM)

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Methods: We studied BU PK, engraftment and survival in children who underwent allogenic BMT for NM (n = 33) or AL (n = 41) after BU-based conditioning. The dose of oral BU was 4 mg/kg (n = 16) or 150 mg/m^2 (n = 32) and intravenous (IV) 3.2 mg/kg (n = 3), 120 mg/m^2 (n = 3) or 130 mg/m^2 (n = 20). In 62 cases, blood was collected after the first dose, BU levels were measured and BU area-under-the-concentration-versus-time curve (AUC) was determined using the Kinetica software (Innaphase, USA), then normalized to 130 mg/m^2 for IV BU and 150 mg/m^2 for oral BU. PK-guided dose adjustments were made in 7 patients with NM. Total exposure to BU was determined by dividing first dose AUC by first dose (mg) and then multiplying by the total dose (mg) administered. **Results:** In the NM group, 26(79%) are still alive. 5 (of 7) deaths occurred early (<118 d post BMT) due to transplant-related causes: VOD (1), VOD and GVHD (2), GVHD (1) and sepsis (1). Full engraftment was achieved in all but 5 patients (85%): 2 had stable mixed chimerism (MC) >95% donor, 3 had inadequate engraftment; 4 of these were part of a group of 12 who had T cell depletion. Total Bu exposure ranged from 57 to 146 mg/L.h (median 90 mg/L.h). In the AL group, 29 (71%) are still alive, with 4 early transplant-related deaths from GVHD (2), relapse (1) and sepsis (1). Full engraftment was achieved in all but 3 patients (93%): 2 children had MC and one of these subsequently lost the graft, another was fully donor but died prior to obtaining full haematological recovery. Total Bu exposure ranged from 40 to 345 mg/L.h (median 99 mg/L.h). Results of the normalised AUC (nAUC) in mg/L.h are shown in the table. nAUC was significantly higher in the oral BU group (n = 36) than in the IV BU group (n = 26): 27 $\pm$ 6 mg/L.h versus 23 $\pm$ 8 mg/L.h, $p < 0.01$. **Conclusions:** Single daily dose BU is generally safe and effective for use in children with AL and NM. A dose of 130 mg/m^2 IV gives less exposure than 150 mg/m^2 oral. Wide variability in BU pharmacokinetics indicates a need for measurement and perhaps targeting in some patients, especially those with immune deficiencies or those more likely to reject.

normalised AUC (nAUC) mg/L.h

Diagnosis:	Genetic	SCID	non-SCID	AL
IV Bu				
nAUC (range)	20–44	14–50	18–31	14–30
median	23	16	21	18
fold variation	2.2	3.6	1.9	2.2
n	6	3	7	10
Oral Bu				
nAUC (range)	15–38	18–25	27–36	15–43
median	25	25	30	28
fold variation	2.5	1.4	1.3	2.9
n	9	3	4	20

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FUNGAL INFECTIONS: A SURVEY OF PEDIATRIC SURVEY OF PEDIATRIC BLOOD & MARROW TRANSPLANT CONSORTIUM INSTITUTIONS

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This survey was designed to identify the fungal infection management used for the pediatric BMT patient and to develop a standard of care for fungal infection management by institutions within the Pediatric Blood & Marrow Transplant Consortium (PBMTC).

Twenty five percent of the surveys were returned. 100% of the institutions performed allogeneic and autologous transplants. Nonmyeloablative transplants were performed by 89% of the institutions.

All institutions used some type of fungal prophylaxis during transplant, 77% used fungal prophylaxis on all their transplant patients. 50% of the centers differed on the prophylaxis used in the BMT sub-groups, with 85% of the centers using Fluconazole, and 15% of the institutions using no prophylaxis in autologous patients. 100% of centers administered prophylaxis to the allogeneic transplant group. The break down of agents utilized in the allo-graft group was Fluconazole (47%), Voriconazole (23%) and low dose